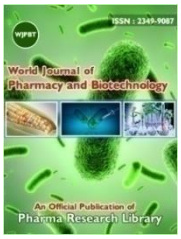

World Journal of Pharmacy and Biotechnology
Home Page: https://pharmaresearchlibrary.org/journals/index.php/wjpbt
e-ISSN: 2349-9087 | Publisher: Pharma Research Library
W. J. Pharm. Biotech., 2025, 12(2): 92-101
DOI: https://doi.org/10.30904/j.wjpbt.2025.4904

Development and Evaluation of Ophthalmic Drug Delivery System for Glaucoma

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A B S T R A C T
This study aimed to develop ocuserts of Pefloxacin mesylate using various polymers (PVA, HPMC, PVP, and HEC) through solvent casting. The resulting films were smooth and transparent, although variations in thickness were observed. The formulation PD3, containing HEC, demonstrated high moisture absorption, while PA1 exhibited moisture loss. The ocuserts had a thickness ranging from 0.14±0.022mm to 0.225±0.045mm and weights from 10.14±0.12mg to 17.25±0.11mg. In vitro drug release studies of PD3 indicated prolonged release, with approximately 47.2% of the drug released within 12 hours, following zero-order kinetics. Ex vivo studies of PD3 showed a release of approximately 51.3%. The developed ocuserts displayed controlled release properties and uniform characteristics, suggesting their potential as an effective ophthalmic delivery system for Pefloxacin mesylate, reducing dosing frequency and improving patient compliance.
Keywords: Orally disintegrating tablets, Clozapine, Ludiflash, FTIR.

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Article History
Received 22 July 2025
Revised 10 Aug 2025
Accepted 11 Sep 2025
Published 31 Oct 2025

Citation: Komata Sharon, *et al.* Development, Development and Evaluation of Ophthalmic Drug Delivery System for Glaucoma, W. J. Pharm. Biotech., 2025, 12(2): 92-101.

C O N T E N T S

1. Introduction

The formulation of ocular drug delivery poses a challenge to researchers. When a drop of an aqueous solution is applied to the eye, regardless of the volume, it is completely eliminated within 5 to 6 minutes. Only a small percentage (1-3%) of the solution actually penetrates the cornea and reaches the intraocular tissue. A recent trend in ocular research aims to develop dosage forms that not only extend the duration of drug presence in the eye but also minimize drug elimination.[1-5] Over the past few decades, there has been significant advancement in the development of new ocular dosage forms, and their utilization is expected to increase in the near future. Ophthalmic inserts offer several advantages compared to conventional dosage forms, including prolonged residence in the eye, controlled and sustained release of drugs, accurate dosing, elimination of preservatives, and increased shelf life. The design, construction, and technology of ocular inserts as controlled and sustained delivery devices are rapidly improving to overcome these limitations.[8] Pefloxacin mesylate is a synthetic broad-spectrum fluoroquinolone antibacterial agent effective against both gram-negative and gram-positive bacteria. The release of the drug through polymer films depends on the properties of the polymers and plasticizers. In this study, different ratios of polymers were blended to combine their individual advantages. The objective of this study was to prepare Pefloxacin mesylate Ocuserts using various proportions and combinations of

different polymers (HPMC, HEC, PVA, and PVPK-30).

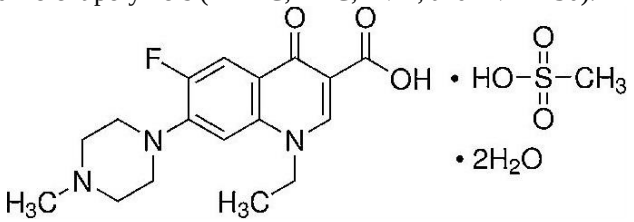

Fig.1: Pefloxacin mesylate

Name of the drug : Pefloxacin mesylate
Chemical Name: 1-ethyl-6-fluoro-7-(4-methylpiperazin-1-yl)-4-oxoquinoline- 3-carboxylic acid;methanesulfonic acid
Formula: $C_{18}H_{24}FN_3O_6S$
Molecular weight: 429.5
Category : Anti-bacterial agents
Solubility : Water-soluble
Melting point : 60^{O}C
About : Pefloxacin, fluoroquinolone antibiotic, is utilized primarily for treating bacterial infections, such as pneumonia, typhoid fever, urinary tract infections, and gonorrhea. Bacterial infection refers to the presence of bacteria within the body, leading to infection. These infections can affect various body parts and spread rapidly. Pefloxacin contains Pefloxacin, an antibacterial agent that effectively treats and prevents a wide range of bacterial infections. It acts by killing the bacteria responsible for the infections and inhibiting their cell repair process. Consequently, it prevents the further spread of the infection. Pefloxacin exhibits broad-spectrum activity against most Gram-negative bacteria, many Gram-positive bacteria, and certain anaerobic bacteria that thrive without oxygen.

Pharmacokinetics parameters:
Absorption : Oral
Protein binding : 20-30%
Metabolism : Liver
Route of elimination : Kidney
Half life : 8.6Hrs
Log P : 0.27
Solubility : 11.4mg/ml at 25^{O}C
Uses: Treatment of bacterial infections
Side effects: Nausea, headache, diarrhea, vomiting, itching, dizziness

Drug-Drug Interaction:
Pefloxacin may interact with antidiabetic medicines (glimepiride, glipizide, glyburide, metformin, tolazamide, chlorpropamide and tolbutamide) and blood thinners (aspirin, warfarin). It may also interact with medicines used for asthma (theophylline).

2. Materials and Methods

Table.1: Equipment used

Materials	Manufacturer
UV-Visible	Schimadzu
Vernier Caliper	Mitutoyo
Laboratory hot air oven	Sansel
Electronic balance	Cyber lab
Magnetic stirrer	REMI equipment pvt. Ltd
pH meter	Susima Technologies (p) Ltd

Table.2: Materials used

Materials	Suppliers
Pefloxacin	Yarrow chemicals Pvt. Ltd.
Poly vinyl alcohol	Qualigens fine chemicals, Mumbai
Hydroxy propyl methyl cellulose	Loba chemicals PVT. LTD, Mumbai
Hydroxy ethyl cellulose	LAB chemicals, Chennai
PVPK-30	Dabur, India
Ethyl cellulose	Yarrow chemicals Pvt. Ltd.
Di-butyl phthalate	Sigma Aldrich

Table.3: Description of solubility

Descriptive term	Parts of solvent required for 1 part of solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1,000
Very slightly soluble	From 1,000 to 10,000
Practically insoluble	Greater than or equal to 10,000

Standard curve for Pefloxacin mesylate:
Preparation of a pefloxacin calibration curve in a pH 7.4 phosphate buffer. The medication was precisely weighed at 100 mg per 100ml. 1 ml of this solution is pipetted into a 10ml volumetric flask. The solution's volume was raised to 10ml. The solution was labelled a stock solution. Stock solutions were generated in concentrations of 0g/ml, 1g/ml, 2g/ml, 3g/ml, 4g/ml, and 5g/ml. The above-prepared solutions were viewed in a UV-Spectrophotometer at 273 nm in increasing order of concentration, and absorbance was determined.

Drug-excipient compatibility study:
Fourier transfer infrared spectroscopy (FTIR)
To assess medication excipient compatibility, FTIR analysis is utilised. The combination of dried medication, natural polymer, and KBr (used as a dispersion medium) was run. Compatibility is established when the acquired spectra of drug and natural polymer match the spectra of pure drug. If the spectra of a drug excipient do not match those of the pure drug, the drug and polymer are incompatible.

Preparation of ocuserts using different polymers:
The Ocusert of pefloxacin was prepared through the following three steps: The drug reservoir was prepared by dissolving 1.0, 2.0, and 4.0% of HPMC, PVA, HEC PVP K-30, along with 0.38% of pefloxacin mesylate (PM) and Di-butyl phthalate (30%, w/w) in doubly distilled water. The solution was poured into a glass ring placed in a Teflon coated Petri dish. The solvent was evaporated by keeping it in an oven at 35 ± 2°C for 24 hours. The rate controlling membranes were prepared by dissolving a specific amount of polymer in ethanol. The solution was poured into a glass ring placed on mercury as a substrate in a petri dish. A portion of the solution was dried in a hot air oven at 40ºC for 48 hours. The resulting dried films were collected.

The drug reservoir was sandwiched between two rate controlling membranes. Chloroform was applied to the edges of the membranes to seal them, ensuring controlled release from the periphery. Elliptically shaped ocular inserts were cut from the medicated reservoir film using a stainless steel die. These inserts were then placed between two rate controlling membranes. The membranes containing the reservoir film were exposed to ethanol/acetone vapors for 1–2 minutes, resulting in a sealed ocular insert. Each insert contained 0.72 mg of the drug. The ocular inserts were stored in an airtight container under normal conditions.

Evaluation test for prepared pefloxacin ocuserts:

Physical evaluation: Ocusert film was examined in terms of characteristics, form, colour, texture, and appearance.

Weight variation: To ensure weight homogeneity, three films from each batch were chosen at random and their weights were assessed using an electronic balance.

Thickness: Using a screw gauge, the thickness of the ocuserts was measured, and the average thickness of three films was estimated.

Uniformity of content: Three films from each batch were dissolved or crushed in 10ml of isotonic phosphate buffer (pH 7.4) in a beaker, filtered into a 25ml volumetric flask, and the volume was filled up with buffer. After taking one ml of the aforesaid sample, the absorbance was measured using a UV-VIS spectrophotometer at 273nm suitable dilutions.

Percentage moisture absorption:

Three strips were precisely weighed and put in an aluminium chloride-containing desiccator. After three days, the strips were reweighed, and the % moisture absorption was measured using the formula below.

$$\% \text{ Moisture absorption} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \text{ X } 100$$

Percentage of moisture loss:

Three strips were precisely weighed and put in a desicator containing either calcium chloride or silica gel. After three days, the strips were reweighed, and the % moisture absorption was measured using the formula below.

$$\% \text{ Moisture loss} = \frac{\text{Initial weight} - \text{ Final weightt}}{\text{Initial weight}} \text{ X } 100$$

Folding Endurance was measured by folding a short strip of film repeatedly until it broke. Folding endurance is determined by the number of times it was folded before it broke.

Surface pH: The inserts were allowed to swell for 30 minutes in 0.1 ml of bi distilled water in a closed petridish at room temperature. To estimate the surface pH, the swollen device was removed and put under a digital pH metre (Elico, India).

Swelling index:

Three ocuserts were weighted and individually put in beakers containing 4 ml of artificial tear fluid. After 5 minutes, the ocuserts were removed and the surplus water was wiped off and weighed. The % swelling index was computed as follows:

(Weight of swollen insert after time – original weight of insert at zero time) × 100

Water vapor transmission:

The transmission cells were rinsed and dried in vials of equal diameter. In the cells, 1gm of fused calcium chloride was placed, and the films were cemented over the brim with solvent. The cells were then precisely weighed and stored in closed desiccators containing a saturated solution of potassium chloride (200 ml), with the cells being removed and weighed after 1,2,3,4,5,6, and 7 days of storage. The water vapours transferred were then computed using the procedure below.

$$\text{WVT Rate} = \frac{WL}{S}$$

W - Gm of water transmitted

L - Thickness of film

S - Exposed surface area of film

***In vitro* release studies through artificial membrane**

The bi-chambered donor receiver compartment model (Franz diffusion cell) was used for in-vitro release investigations. The membrane of the diffusion cell (pre-hydrated cellophane) was connected to one end of the open cylinder, which served as the donor compartment. The ocular implant was put on a dialysis membrane that was in touch with receptor media (pH=7.4). A magnetic stirrer was used to continually mix the receptor compartment's contents, and the temperature was maintained at 370 0.50 C. To replicate eyelid blinking, the receptor media was continually swirled at 20rpm. At regular intervals, a 3ml aliquot of the solution was taken and replaced with new STF, and the necessary dilutions were prepared. The aliquot was tested for drug content using a UV Spectrophotometer at 273 nm and a reference standard of simulated tear fluid as a blank.

Ex-vivo trans corneal permeation studies:

The current study conducted drug release experiments in vitro, with triplicate measurements. At various time intervals, samples were collected, and the cumulative percentage of drug release was calculated based on the average drug amount present in the respective ocular insert. A whole goat eyeball was obtained from a local butcher shop and promptly transported to the laboratory in cold normal saline (4°C) within one hour of the animal's slaughter. The cornea, along with 2 to 4 mm of surrounding scleral tissue, was carefully excised and rinsed with cold normal saline until the washing was free from proteins. The isolated cornea was then mounted in a modified all-glass Franz diffusion cell, with the surrounding scleral tissue clamped between the donor and receptor compartments, ensuring that the cornea's epithelial surface faced the donor compartment. The receptor compartment was filled with 20 ml of freshly prepared STF solution. An ocular film measuring one square cm was placed on the cornea, and the opening of the donor compartment was sealed with a glass cover slip. The receptor fluid was maintained at 35ºC with constant stirring, using a Teflon-coated magnetic stir bead. A 3ml sample was withdrawn from the receptor compartment at different time intervals, up to 24 hours, and analysed spectrophotometrically at 273nm

Release kinetics of the optimized formulations

Drug Release Kinetics

The data from the in vitro release research was applied to various motor circumstances. Zero request (aggregate level of medication discharge versus time), first request (log total level of medication remaining versus time), Higuchi model (total level of medication discharge versus square base of time), and Korsmeyer-Peppas (log combined percent sedate delivery versus log of time) were the active models used. Relapse (r2) values were calculated for the direct bends obtained from relapse research.

Kinetic analysis: The grid frameworks were accounted for in order to follow the zero-request discharge rate and the Diffusion component for pharmaceutical arrival. The information obtained was fitted into the Zero request, First request, Higuchi lattice, and Peppa's model to break down the system for the delivery and delivery rate energy of the measurements structure. The best fit model was picked in this case based on the r Values obtained.

Kinetics of zero order:

The following equation can be used to depict drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the medication slowly, provided that the area does not change and no equilibrium conditions are established.

$$Qt = Q0+K0t$$

Where Qt represents the quantity of drug dissolved in time t, Q0 represents the starting amount of drug in the solution, and Ko represents the zero order release constant.

To investigate first order release kinetics, the release rate data were fitted to the following equation.

$$Qt = \log Q0 + k1t/2.303.$$

Where Qt represents the quantity of drug released in time t, Qo represents the initial amount of drug in the solution, and K1 represents the first order release constant.

Higuchi model: Higuchi created many theoretical models to investigate the release of water-soluble and low-soluble medicines integrated in semisolids and/or solid matrices. For drug particles distributed in a uniform matrix acting as a diffusion medium, mathematical formulas were developed. And the formula is Qt = KH.t1/2.

Where Qt represents the quantity of medication released in time t and KH represents the Higuchi Dissolution constant.

The Korsmeyer and Peppa model:

To investigate this concept, the following equation is fitted to the release rate data.

$$Mt/M = Ktn$$

Where Mt/M is the drug release percentage, K is the release constant, t is the release period, and n is the drug release diffusion exponent that depends on the geometry of the matrix dosage form.

Table.4: Diffusion exponent and solute release mechanism for cylindrical shape Diffusion

Diffusion coefficient	**Overall solute diffusion mechanism**
0.45	Fickian diffusion
0.45<n<0.89	Anomalous (non-fickian diffusion)
0.89	Case II transport
n>0.89	Super Case II transport

Table.5: Composition of the reservoir films

Ingredients	PA1	PA_2	PA_3	PB_1	PB_2	PB_3	PC_1	PC_2	PC_3	PD_1	PD_2	PD_3
Pefloxacin (%m/V)	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38
HPMC (%)	1	2	4	-	-	-	-	-	-	-	-	-
PVA(%)	-	-	-	1	2	4	-	-	-	-	-	-
PVPK-30 (%)	-	-	-	-	-	-	1	2	4	-	-	-
HEC (%)	-	-	-	-	-	-	-	-	-	1	2	4
Dibutyl phthalate (%)	30	30	30	30	30	30	30	30	30	30	30	30
Water (ml)	15	15	15	15	15	15	15	15	15	15	15	15

Table.6: Composition of rate controlling membranes

S.No	**Ingredients**	**Quantity**
1	Ethyl cellulose	1.2%
2	Dibutyl phthalate (% w/w)	30%
3	Ethanol (ml)	15

3. Results and Discussion

Table.7: Solubility of Pefloxacin mesylate

Solvent	**Solubility**
Water	Very slightly soluble
Alcohol	Very slightly soluble
Chloroform	Very slightly soluble

Organoleptic properties: Pefloxacin comes in the form of a white or light yellow powder.

Melting point: Pefloxacin mesyalte is 255^{O}C.

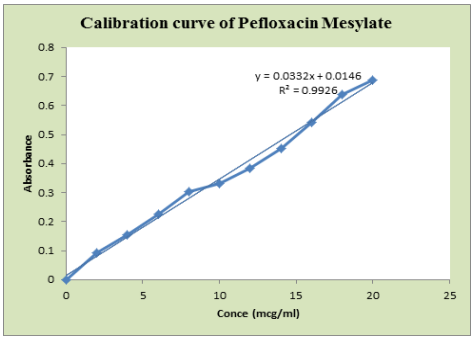

Fig.2: Calibration curve of Pefloxacin mesylate

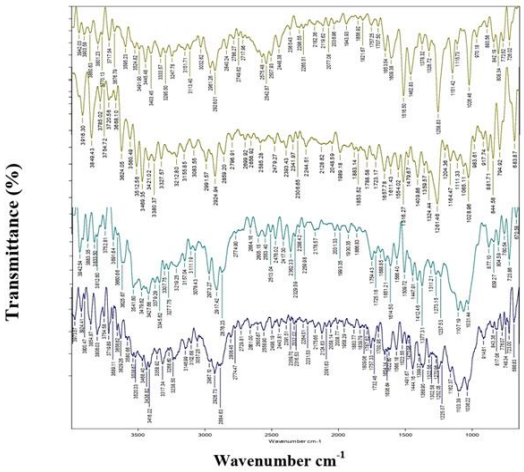

Fig.3: FTIR Spectra of Drug alone and its combination

The IR spectral investigations of the medication and its physical excipient mixes preserved their distinct absorption properties without interfering with one another. We may infer from this investigation that no unexpected chemical reactions occurred while doing this research. There is no interaction between the medication and the polymer. Figure no.8.2 depicts the infrared spectra of pure drugs and physical mixes.

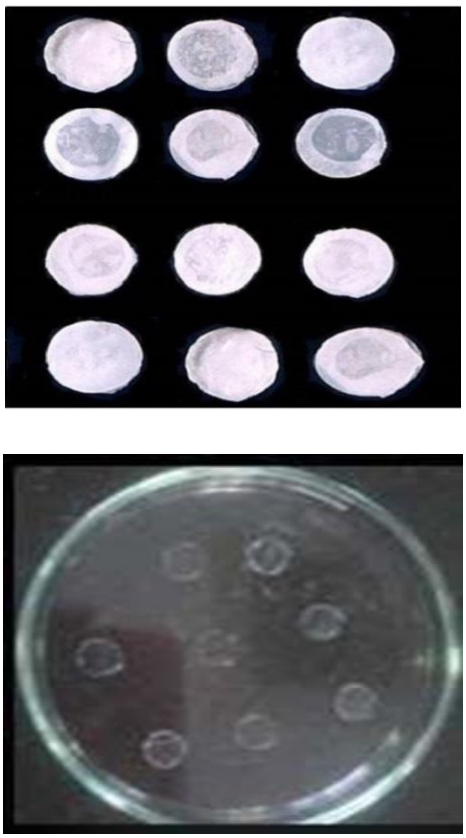

Fig.4: Prepared ocuserts

Formulation of Pefloxacin mesylate ocuserts:

Pefloxacin mesylate ocuserts were created by combining various polymers in varying quantities with dibutyl phthalate as a plasticizer. The solvent casting procedure is used to make occuserts.

Evaluation test for prepared pefloxacin mesylate ocuserts:

Physical assessment: The prepared ocuserts have a round shape, a yellowish white colour, a homogeneous look, and a smooth texture**.**

Weight variation: The weight of each batch of ocular films was determined to be uniform and within the range (Table No.). The weight homogeneity of the films suggests that the polymer, medication, and plasticizer were distributed evenly.

Table.8: Physical evaluation and weight variation studies of pefloxacin mesylate ocuserts

Formulation	Weight (mg)	Thickness (µm)
PA1	15.39±0.24	0.14±0.022
PA2	12.47±0.62	0.16±0.078
PA3	13.95±0.47	0.14±0.089
PB1	10.14±0.12	0.21±0.057
PB2	16.27±0.11	0.24±0.011
PB3	14.74±0.34	0.25±0.023
PC1	15.69±0.24	0.20±0.065
PC2	14.35±0.47	0.22±0.074
PC3	11.41±0.85	0.21±0.054
PD1	15.36±0.63	0.18±0.012
PD2	16.54±0.78	0.22±0.057
PD3	17.25±0.11	0.25±0.045

Content uniformity:

The Drug content was found consistent in all formulations and varied from 92.25 ±0.03% and 99.98±0.02%.

Percentage moisture absorption:

The moisture absorption percentage was estimated for each of the 12 formulations. A positive linear association was discovered between moisture absorption capacity and the concentration of hydrophilic polymers. As the concentration of hydrophilic polymers grew, so did the percentage of moisture absorption.

Percentage of moisture loss:

The percentage moisture loss was determined for each of the 16 formulations. A significant linear link was discovered between moisture absorption capacity and the concentration of hydrophilic polymers PVA and HPMC. As the concentration of PVA and HPMC grew, so did the percentage moisture loss.

Folding endurance: Folding endurance was personally tested for all formulations. It was discovered in the range of 187.33 to 3083.74. This test demonstrates the adaptability of ocuserts. This test verifies that the produced ocuserts are appropriate for large-scale production of lengthy, continuous film that does not break or rip.

Surface pH: The surface pH of the produced ocuserts ranged from 7.130.27 to 7.890.15. All formulations' surface pH was determined to be close to tear fluid pH.

Swelling index:

The swelling index was determined to be between 3.510.33 to 6.250.15. The results revealed that the produced ocuserts swelled well and that there was no significant change in the absorption characteristics of the formulations.

Water vapor transmission: The water vapor transmission was found in the range of 1.532±0.07 to 2.235±0.08. The

result showed good water vapor transmission of the prepared ocuserts.

***In vitro* release studies through artificial membrane:**

Ocuserts were chopped to size and put in a diffusion cell between the donor and receptor compounds. Pre-hydrated cellophane was employed as a semipermeable membrane as a support beneath the ocuserts film STF was used as the medium. The setup was operated for 12 hours at 20rpm with sample intervals of 1,2,3,4,5,6,7,8,9,10,11. The amount of medication released was calculated using a UV spectrophotometer to measure absorbance.

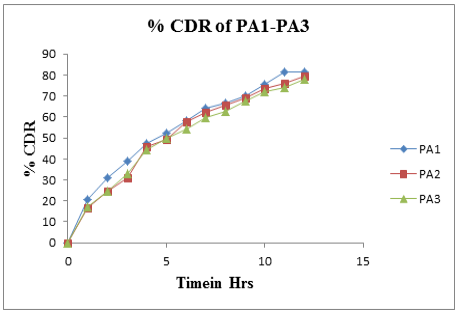

Fig.5: % Cumulative drug release of PA1-PA3

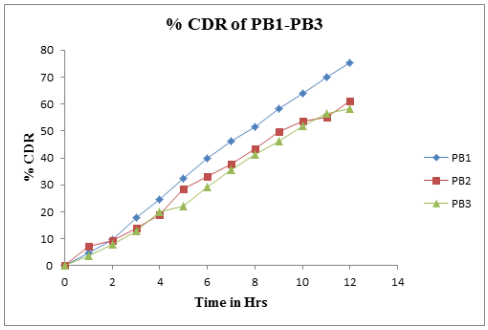

Fig.6: % Cumulative drug release of PB1-PB3

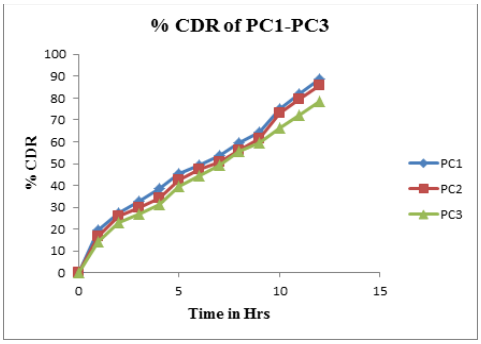

Fig.7: % Cumulative drug release of PC1-PC3

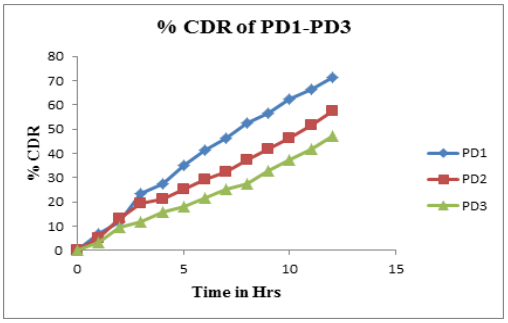

Fig.8: % Cumulative drug release of PD1-PD3

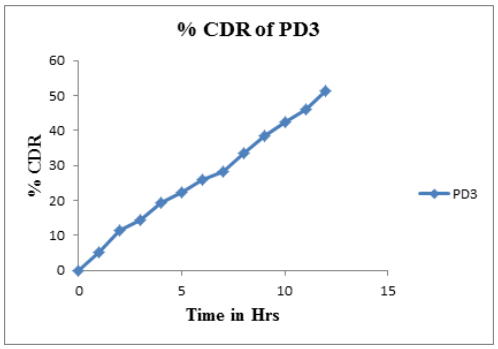

Fig.9: % Cumulative drug release by Ex-vivo of PD3

Drug release kinetics:

To investigate the kinetics of drug release, the release constants were calculated by analyzing the slopes of the corresponding plots. The results of all formulations, which demonstrated superior physicochemical characteristics and release behavior compared to others (as depicted in Figure No.), were summarized in Table 4. The best formulation of ocular films exhibited a higher correlation (r2 > 0.99) with zero-order plots, as determined through regression analysis. Zero-order plots confirmed the slow diffusion of the drug from the ocular films. Applying the Korsmeyer-Peppas model in planar geometry, a value of n = 0.5 indicated Fickian diffusion, while 0.5 < n < 1.0 indicated anomalous (non-Fickian) transport, and n = 1 indicated case II (relaxation-controlled) transport. In the present films, the observed values ranged from 0.629 to 0.933, indicating that the release mechanisms followed anomalous (non-Fickian) transport and zero-order release.

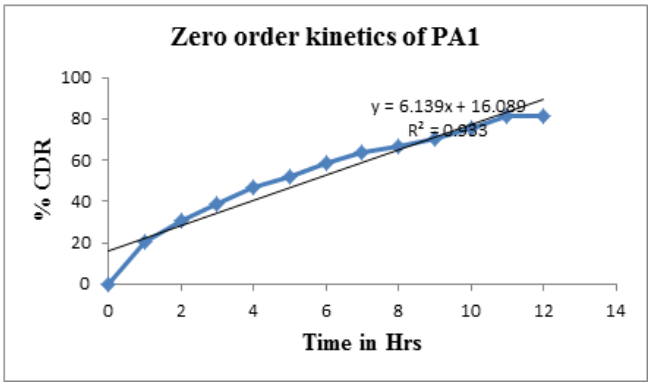

Fig.10: Zero order kinetics of Formulation PA1

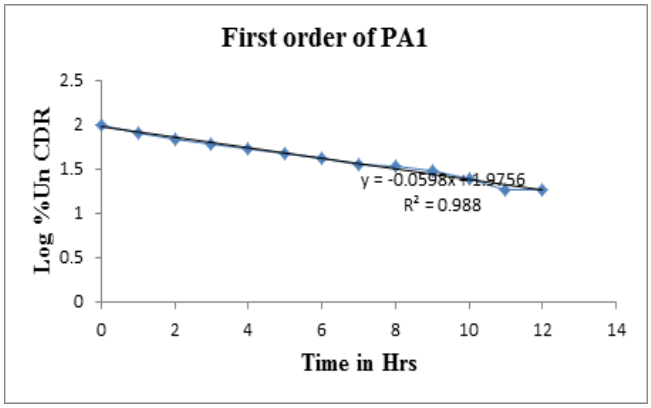

Fig.11: First order kinetics of Formulation PA1

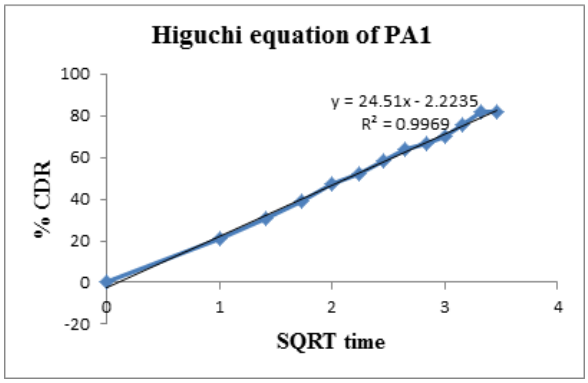

Fig.12: Higuchi kinetics of Formulation PA1

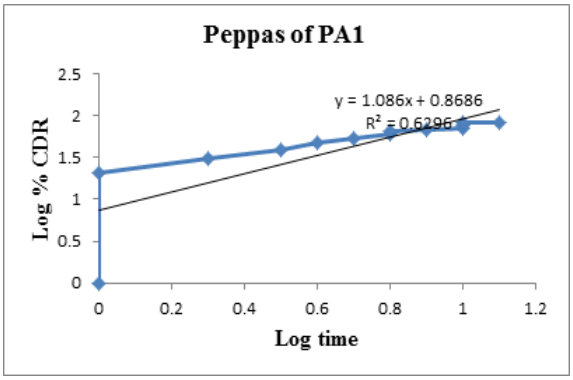

Fig.13: Peppas equation of Formulation PA1

Table.9: % Drug content, % Moisture absorption and % Moisture loss studies of pefloxacin mesylate ocuserts

Formulation	% Drug content	% Moisture absorption	% Moisture loss
PA1	92.25±0.01	5.54 ± 0.231	4.04±0.41
PA2	93.77±0.05	6.74 ± 0.141	5.78±0.37
PA3	98.43±0.06	9.77 ± 0.452	8.23±0.31
PB1	91.69±0.02	5.24 ± 0.385	4.41±0.21
PB2	94.66±0.07	7.78 ± 0.774	5.28±0.37
PB3	97.43±0.05	8.52 ± 0.652	8.78±0.05
PC1	92.79±0.07	6.74 ± 0.174	4.17±0.70
PC2	95.78±0.05	8.89 ± 0.125	6.95±0.11
PC3	96.89±0.02	10.45 ± 0.241	9.41±0.23
PD1	93.75±0.04	11.17 ± 0.447	5.34±0.21
PD2	96.64±0.03	12.87 ± 0.325	6.46±0.58
PD3	99.79±0.07	13.99 ± 0.714	8.73±0.04

Table.10: Folding endurance, Surface pH, swelling index and WVT of Pefloxacin mesylate ocuserts

Formulation code	Folding endurance	Surface pH	Swelling index	Water vapor transmission (Rate X 10^3) $mg.cm^{-2}h^{-1}$ (Mean±SD)
PA1	187±2.33	7.13±0.27	3.51±0.33	1.531±0.07
PA2	257±1.35	7.43±0.12	4.72±0.12	1.843±0.04
PA3	297±2.37	7.71±0.52	6.20±0.58	2.125±0.07
PB1	193±1.53	7.25±0.13	3.85±0.14	1.571±0.08
PB2	224±0.88	7.51±0.56	4.12±0.25	1.812±0.02
PB3	302±3.14	7.89±0.45	6.99±0.36	2.214±0.06
PC1	199±2.14	7.71±0.13	4.57±0.96	1.552±0.01
PC2	2.66±1.58	7.23±0.11	5.23±0.75	1.913±0.02
PC3	291±2.12	7.82±0.35	6.14±0.18	2.225±0.03
PD1	207±1.52	7.62±0.12	3.27±0.29	1.532±0.07
PD2	287±2.13	7.77±0.28	5.72±0.63	1.857±0.02
PD3	308±3.74	7.87±0.36	6.25±0.15	2.235±0.06

Table.11: In-vitro drug release profile of pefloxacin mesylates ocuserts prepared with HPMC

Time in Hrs	PA1	PA_2	PA_3
0	0	0	0
1	20.8	16.8	17.2
2	30.8	24.4	24.5
3	38.8	31.2	32.8
4	47.2	45.8	44.5
5	52.4	49.1	49.6
6	58.4	57.6	54.3
7	64.2	62.3	59.7
8	66.5	65.8	62.5
9	70.1	69.1	67.5
10	75.5	73.5	71.9
11	81.6	76.2	74.3
12	81.7	79.3	77.8

Table.12: In-vitro drug release profile of pefloxacin mesylates ocuserts prepared with PVA

Time in Hrs	PB1	PB2	PB3
0	0	0	0
1	4.8	7.2	3.5
2	9.6	9.2	7.9
3	17.8	14	12.8
4	24.4	18.8	19.8
5	32.3	28.4	22.1
6	39.8	33.2	29.1
7	46.2	37.7	35.6
8	51.5	43.2	41.4
9	58.4	49.8	46.2
10	64.1	53.7	51.8
11	69.9	55.2	56.4
12	75.2	61.1	58.2

Table.13: In-vitro drug release profile of Pefloxacin mesylates ocuserts prepared with PVP K-30

Time in Hrs	PC1	PC2	PC3
0	0	0	0
1	19.7	16.9	14.2
2	27.2	25.8	23.1
3	32.5	29.8	26.7
4	38.7	34.3	31.3
5	45.2	42.3	39.4
6	49.5	47.5	44.2
7	53.7	50.7	49.1
8	59.3	56.2	55.5
9	64.5	61.3	59.6
10	75.2	72.9	66.4
11	81.8	79.3	72.1
12	88.7	85.7	78.4

Table.14: In-vitro drug release profile of Pefloxacin mesylates ocuserts prepared with HEC

Time in Hrs	PD1	PD2	PD3
0	0	0	0
1	6.7	5.2	3.2
2	11.9	13.3	9.5
3	23.3	19.3	11.6
4	27.5	21.3	15.6
5	35.1	25.2	18.2
6	41.2	29.4	21.5
7	46.1	32.4	25.1
8	52.6	37.2	27.6
9	56.5	41.8	32.7
10	62.5	46.5	37.2
11	66.3	51.6	41.8
12	71.4	57.6	47.2

Table.14: Drug release kinetics of formulation PA1

Time in Hrs	Sqrt time	Log time	% CDR	Un CDR	log% un CDR	Log % CDR
0	0	0	0	100	2	0
1	1.00	0.0	20.8	79.2	1.90	1.32
2	1.41	0.3	30.8	69.2	1.84	1.49
3	1.73	0.5	38.8	61.2	1.79	1.59
4	2.00	0.6	47.2	52.8	1.72	1.67
5	2.24	0.7	52.4	47.6	1.68	1.72
6	2.45	0.8	58.4	41.6	1.62	1.77
7	2.65	0.8	64.2	35.8	1.55	1.81
8	2.83	0.9	66.5	33.5	1.53	1.82
9	3.00	1.0	70.1	29.9	1.48	1.85
10	3.16	1.0	75.5	24.5	1.39	1.88
11	3.32	1.0	81.6	18.4	1.26	1.91
12	3.46	1.1	81.7	18.3	1.26	1.91

4. Conclusion

Successful preparation of ocular films containing Pefloxacin mesylate was achieved through solvent casting using PVA, PVP, HPMC, HEC at varying concentrations. Di-butyl phthalate was used as a plasticizer. These findings indicate that the PD3 formulation of Pefloxacin mesylate has a significant impact on the physicochemical characteristics and permeability properties of the polymer films. These films possess satisfactory strength and safety, leading to reduced frequency of administration and improved patient compliance. Consequently, these films can be utilized in ophthalmic formulations. The ocular films exhibited smooth, flexible, and uniform characteristics in terms of thickness and weight. They demonstrated controlled release properties, with a zero-order drug release pattern. Therefore, the developed ocuserts hold promise as a delivery system for Pefloxacin mesylate, providing controlled drug release. Overall, the ocular insert successfully addresses issues related to frequent dosing and active ingredient wastage.

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Source of Support: Nil.